UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

FEB 14 2013

MEMORANDUM

SUBJECT: Guidance for Residues of Concern in Drinking Water

FROM: Donald J. Brady, Ph.D., Director
Environmental Fate and Effects Division (7507P)
Office of Pesticide Programs

TO: Environmental Fate and Effects Division (7507P)
Office of Pesticide Programs

The purpose of this guidance, which is effective immediately, is to assist Environmental Fate and Effects Division (EFED) scientists in determining pesticide residues of concern in drinking water in coordination with Health Effects Division (HED) scientists and HED's Residues of Concern Knowledgebase Subcommittee (ROCKS). EFED scientists assess exposure to pesticide residues of concern in drinking water in order to support human health dietary risk assessments. Implementing this guidance should help EFED scientists interact more uniformly with HED scientists and should result in more robust and consistent rationales for drinking water residues of concern.

This guidance supersedes previously released guidance and addenda (dated March 17, 2008, August 26, 2008, and May 10, 2011) on this subject. Guidance Attachments 1 and 2 were developed by EFED's ROCKS representatives. Attachments 3 and 4 were developed by HED's ROCKS representatives in collaboration with Christina Swartz and EFED ROCKS representatives. For further information, please contact Greg Orrick or other EFED ROCKS representatives.

EFED ROCKS Representatives

Reuben Baris, Environmental Scientist
Brian Kiernan, Biologist
Greg Orrick, Environmental Scientist
Mah T. Shamim, Ph.D., Branch Chief
Katrina White, Ph.D., Biologist

Attachments

Attachment 1: EFED Guidance for Drinking Water Residues of Concern
Attachment 2: EFED ROCKS Memorandum Template
Attachment 3: EFED/HED Process for Registration Review Collaboration on Drinking Water Residues of Concern
Attachment 4: Flowchart for the EFED/HED Process for Registration Review Collaboration on Drinking Water Residues of Concern

EFED Guidance for Drinking Water Residues of Concern
January 2013

This Environmental Fate and Effects Division (EFED) guidance document describes the process for identifying drinking water residues of concern in coordination with the Health Effects Division (HED) chemical team and the Residues of Concern Knowledgebase Subcommittee (ROCKS). Residues of concern in drinking water should be identified with supporting rationale by EFED and HED scientists prior to the assessment of drinking water exposure. The ROCKS was formed, in part, to facilitate and document this process.

The procedures below should be followed for actions involving new chemicals or older chemicals for which drinking water residue of concern decisions are unavailable or no longer applicable. This procedure includes guidance on scheduling a ROCKS meeting and how to prepare for it. Preparations include writing a memorandum to the ROCKS and being prepared to briefly, verbally summarize it at the meeting.

A. Registration Review Actions

1) For chemicals in registration review, follow the procedures in Attachments 3 and 4. If a ROCKS meeting is needed, also proceed to Section D of this document.

    a) In summary, beginning at the first team meeting and preferably prior to any Focus meeting with the registrant(s), the EFED and HED teams collaborate to determine whether the description of residues of concern in drinking water needs updating and whether the ROCKS needs to be consulted.

    b) If updating is needed, at a minimum, EFED fills out and emails to HED the degradate table from the ROCKS memorandum template (*i.e.*, the table with chemical names, structures, maximum amounts formed, *etc.*).

    c) If the residues of concern and their rationales are revised, the HED team documents this in an email to the EFED team and in HED's scoping document for registration review.

    d) EFED places in the problem formulation for registration review the degradate table that was emailed to HED and a brief description of the drinking water residues of concern, citing HED's document that provides their rationales.

2) In some cases, the residues of concern in drinking water will need to be revisited after the docket is opened, such as after called-in studies are submitted. Until further guidance on this is provided, follow the guidance below for "other registration actions."

B. New Chemical Registration Actions

1) A ROCKS meeting will be scheduled to occur at least one month prior to the deadline for the drinking water exposure assessment. Ideally, the meeting would occur after the submitted studies are finalized. However, it has been typical for the meeting to occur during the secondary review phase, with the caveat that the data are provisional. Proceed to Section D of this document.

C. Other Registration Actions

1) Two or more months prior to the due date for a drinking water exposure assessment, determine whether drinking water residues of concern have been adequately determined by the ROCKS or its discontinued predecessor, the Metabolism Assessment Review Committee (MARC), for the current action.

2) If the drinking water residues of concern have not been adequately determined (*e.g.*, they were not defined for drinking water when the MARC defined them for plants and livestock or new major degradates have been identified following the MARC meeting), notify your Risk Assessment Process Leader (RAPL) and branch chief and contact the HED chemical team (preferably the risk assessor) to reevaluate the residues of concern and their rationales.

3) If the team cannot come to a conclusion, consult with the ROCKS co-chairs to determine whether and when to schedule an ad-hoc ROCKS meeting or electronic review.

4) The ROCKS meeting or electronic review must be scheduled to occur at least one month prior to the deadline for the drinking water exposure assessment. If a meeting is needed and it isn't scheduled in a timely fashion, follow up with the HED chemical team, your branch chief, and the ROCKS executive secretary (currently Elizabeth Holman) to facilitate scheduling that is acceptable to the participants.

    a) Maintain an informal dialog with the HED chemical team regarding whether any minor environmental degradates are of toxicological concern and, therefore, need more characterization for the ROCKS. Proceed to Section D of this document.

D. Preparing for the ROCKS Meeting

1) Following the template in Attachment 2, draft a memorandum for the ROCKS that very briefly summarizes the environmental fate of the pesticide and its environmental transformation products as well as any available ecotoxicity data on the transformation products. This memorandum does not propose which compounds to include as residues of concern in drinking water.

    a) Two to three weeks prior to the scheduled ROCKS meeting, if possible, send the draft memorandum through secondary review within your branch.

b) Notify the HED chemical team which transformation products are major as early as possible so that the HED toxicologist can investigate their toxicity.

2) Submit the peer-reviewed memorandum to your branch chief and all EFED ROCKS representatives for review at least seven business days prior to the scheduled ROCKS meeting, if possible. (The EFED ROCKS representatives are currently Greg Orrick, Reuben Baris, Katrina White, Brian Kiernan, and Mah Shamim.) Two EFED ROCKS representatives will provide feedback within two business days of receipt of the draft and will work with the EFED chemical team if additional information is needed.

3) Submit the final branch chief-signed memo to the EFED Tracking Team and send an electronic copy to the ROCKS co-chairs (currently Christine Olinger and Edward Scollon) at least five business days before the scheduled ROCKS meeting, if possible, and after completion of review within EFED. (The memo will be posted in the HED ROCKS Database under "Briefing Materials".)

4) At the ROCKS meeting, be prepared to very briefly summarize the environmental fate of the chemical, its major transformation products, and any minor products previously determined to be of risk concern. Also, be prepared to very briefly summarize any ecotoxicity data presented on the transformation products and to field questions regarding the studies supporting your memorandum. Proceed to Section E of this document.

E. After the ROCKS Meeting

1) After the ROCKS meeting, a designated ROCKS secretary will send a draft decision memorandum to the EFED and HED chemical teams and the ROCKS representatives for comment. Once this occurs, promptly provide any feedback to the ROCKS secretary. After feedback is received, the draft decision memorandum will be finalized and posted in the OPP Chemistry Database (*i.e.*, OPPIN Chem Docs).

2) Cite the ROCKS decision memorandum in your drinking water exposure assessment where you explain the rationale for the residues of concern. If the HED and EFED chemical teams have reason to update the ROCKS' recommendations, cite in your drinking water exposure assessment the HED risk assessment or other document that provides the updated drinking water residues of concern and their rationales.

Attachment 2

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

[*Current date*]

PC Code: [*code*]
DP Barcode: [*barcode*]

MEMORANDUM

SUBJECT: Data on [*Chemical name*] and Its Environmental Transformation Products in Support of the ROCKS.

FROM: [*Author(s)*]

THRU: [*Author's branch chief*]
[*Other reviewers can also be listed here*]

TO: Christine Olinger, Co-chair
Edward Scollon, Co-chair
Residues of Concern Knowledgebase Subcommittee

[*This document should include a brief introduction, brief characterization of the environmental fate of the pesticide and its transformation products, brief characterization of the available ecotoxicity data on the transformation products, any other pertinent information, a schematic of the environmental fate pathways and a summary table(s) that includes the key data indicated below.*]

This memorandum provides information about [*chemical name*] and its environmental transformation products. The information in this document can be used by the Health Effects Division to determine which environmental transformation products are of risk concern for the drinking water exposure assessment of [*chemical name*] in support of the human health risk assessment. If you have questions about this memorandum, please contact [*author's name*] at [*author's phone number*].

[*Briefly describe the environmental persistence of the pesticide in soil and water. What are the predicted major routes of degradation in the environment (*e.g., *aerobic soil metabolism, hydrolysis,* etc.*)?*]

[*Briefly describe the expected mobility of the pesticide. Is the pesticide volatile? How well does the pesticide bind to soil or sediment (provide K_d, K_{OC}, or Freundlich descriptors)?*]

[*Briefly describe the bioconcentration potential of the pesticide, providing the maximum fish or oyster BCF value and the rate of elimination, if available. If these data are not available, provide the K_{OW} of the pesticide.*]

[*Briefly describe the pesticide transformation products. Identify major and minor transformation products. Provide available information on their mobility and kinetics of formation and decline. Summarize available information on their ecotoxicity (see Appendix A).*]

[*Provide any other pertinent information, such as monitoring data, the effects (if known) of water treatment on the pesticide and its transformation products.*]

[*A schematic of the environmental transformation pathways of the pesticide, including its major transformation products, is recommended. If a major degradation pathway is not pertinent based on the current and proposed use patterns (*e.g.*, photolysis of a compound only used as a seed treatment), then characterize this near the schematic.*]

[*The ROCKS appreciates receiving a meeting handout (in hard copy) with key data summarized on one sheet of paper. This summary is optional and not part of the memorandum that is submitted electronically to the ROCKS. If the meeting handout is opted for, example Appendix B provides a sample two-page format for this one-sheet summary.*]

[*Provide a table or multiple tables populated with the following key data, as available:*

<u>Key data to tabulate</u>

- *The maximum percent of the applied radioactivity of each transformation product for each submitted study in which a transformation product was identified, as well as the interval during which each peak was maintained*

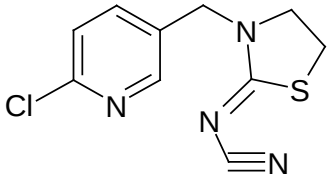
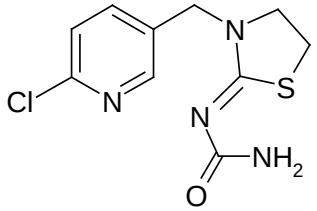
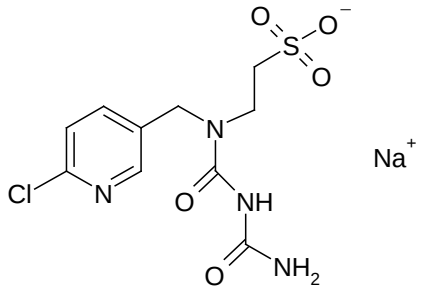
- *The percent of the applied radioactivity of the parent and each transformation product at the final sampling interval of each submitted study in which a transformation product was identified, as well as the duration of each study*

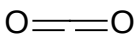
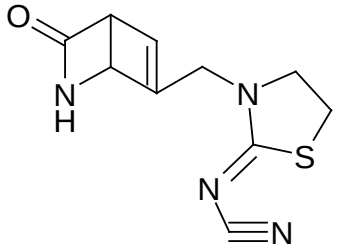
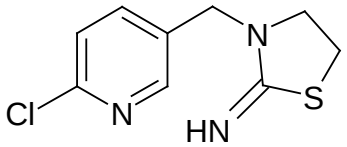
- *The study type, OCSPP guideline, or both and MRID of each identified study*

- *The chemical structure, any common and code names, IUPAC name (CAS name is optional), CAS number, and SMILES string of each identified transformation product*]

[*Further data, such as regressed half-lives of major degradation products, may be reported in the attached tables as available and deemed appropriate. Example Tables 1 and 1.a provide examples of key data presented in single tables. Example Tables 1.b and 1.c provide examples of key data presented across multiple tables. (The ROCKS prefers the format of Example Table 1.) This document should include ALL of the environmental transformation products identified for the pesticide regardless of their characterization level.*]

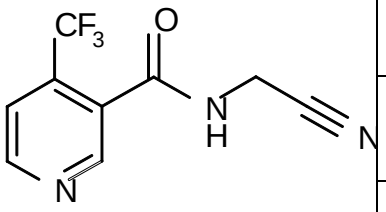
[*Example*] Table 1. Thiacloprid and Its Environmental Transformation Products. [A]

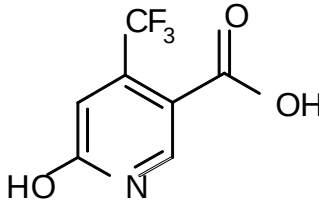
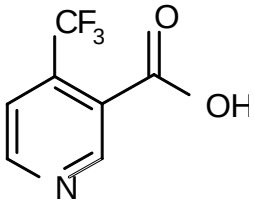
Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (day)
PARENT						
Thiacloprid **YRC 2894**	(*Z*)-3-(6-chloro-3-pyridylmethyl-1,3-thiazolidin-2-ylidenecyanamide **CAS No.:** 111988-49-9 **Formula:** $C_{10}H_9ClN_4S$ **MW:** 252.73 g/mol **SMILES:** ClC1=CC=C(CN2CCSC2=NC#N)C=N1		Aerobic soil	44927916		0.6-1.4 (100-365 d)
			Soil photolysis	44927933		48 (19 d)
			Aqueous photolysis	44927918		84 (18 d)
			Hydrolysis	44927917		95-100 (30 d)
			Aerobic aquatic	44927919		0.5-12 (161-189 d)
				44927920		0.1-9.4 (100 d)
			Anaerobic aquatic	44927935		11-74 (360 d)
			Field studies	44927907		<LOQ (525 d)
				44927908		<LOQ (543 d)
				44927913		<LOQ (539 d)
MAJOR (>10%) TRANSFORMATION PRODUCTS						
Thiacloprid-amide **YRC 2894 amide** **KKO 2254**	(*Z*)-[3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinylidene]urea **Formula:** $C_{10}H_{11}ClN_4OS$ **MW:** 270.74 g/mol **SMILES:** NC(=O)N=C1SCCN1CC2=CC=C(Cl)N=C2		Aerobic soil	44927916	**73.8%** (3 d)	17.1% (100 d)
			Soil photolysis–light	44927933	**23.8%** (19 d)	23.8% (19 d)
			Soil photolysis–dark		**69.6%** (19 d)	69.6% (19 d)
			Aqueous photolysis	44927918	not detected	
			Hydrolysis –pH 4	44927917	not detected	
			Hydrolysis –pH 7		not detected	
			Hydrolysis –pH 9		1.5% (14 d)	nd (31 d)
			Aerobic aquatic	44927919	**64.8%** (10 d)	23.3% (189 d)
				44927920	**69.9%** (35 d)	57.0% (100 d)
			Anaerobic aquatic	44927935	**30.9%** (361 d)	30.9% (361 d)
			Field studies	44927907	45.3% (10 d)	nd (366-525 d)
				44927908	62.8% (6 d)	nd (360-543 d)
				44927913	40.4% (28 d)	11.0% (450 d)
Thiacloprid-sulfonic acid **YRC 2894 sulfonic acid** **WAK 6999 (sodium salt)**	Sodium 2-[[[(aminocarbonyl) amino]carbonyl][(6-chloro-3-pyridiny1)methyl]amino]ethanesulfonate **Formula:** $C_{10}H_{12}ClN_4O_5S$, Na **MW:** 335.75 g/mol, 22.99 g/mol **SMILES:** [Na+].NC(=O)NC(=O)N(CC[S]([O-])(=O)=O)CC1=CC=C(Cl)N=C1		Aerobic soil	44927916	**19.7%** (60 d)	18.6% (100 d)
			Soil photolysis	44927933	not detected	
			Aqueous photolysis	44927918	not detected	
			Hydrolysis	44927917	not detected	
			Aerobic aquatic	44927919	**10.0%** (70 d)	≤0.6% (161 d)
				44927920	**10.1%** (100 d)	10.1% (100 d)
			Anaerobic aquatic	44927935	4.3% (361 d)	4.3% (361 d)
			Field studies	44927907	8.2% (28 d)	nd (58-525 d)
				44927908	7.5% (14 d)	nd (28-543 d)
				44927913	not detected	

Code Name/ Synonym	Chemical Name	Chemical Structure	Study Type	MRID	Maximum %AR (day)	Final %AR (day)
Unextracted residues	(not applicable)	(not applicable)	Aerobic soil	44927916	**30.9%** (365 d)	30.9% (365 d)
			Soil photolysis–light	44927916	9.5% (19 d)	9.5% (19 d)
			Soil photolysis–dark		7.7% (19 d)	7.7% (19 d)
			Aerobic aquatic	44927919	**49.1%** (189 d)	49.1% (189 d)
				44927920	**37.3%** (100 d)	37.3% (100 d)
			Anaerobic aquatic	44927935	**24.7%** (360 d)	24.7% (360 d)
Carbon dioxide	Carbon dioxide **Formula:** CO_2 **MW:** 44.1 g/mol **SMILES:** O=C=O		Aerobic soil	44927916	**34%** (100 d)	34% (100 d)
			Soil photolysis–light	44927916	0.2% (19 d)	0.2% (19 d)
			Soil photolysis–dark		0.3% (19 d)	0.3% (19 d)
			Aqueous photolysis	44927918	not analyzed	
			Hydrolysis	44927917	not analyzed	
			Aerobic aquatic	44927919	**19.6%** (189 d)	19.6% (189 d)
				44927920	4.9% (100 d)	4.9% (100 d)
			Anaerobic aquatic	44927935	3.6% (251 d)	<0.1% (360 d)
MINOR (<10%) TRANSFORMATION PRODUCTS						
WAK 7259 A	(not reported) **Formula:** $C_{10}H_{10}N_4OS$ **MW:** 234.28 g/mol **SMILES:** O=C1NC2C1C=C2CN3CCSC3=NC#N		Aq. photolysis–light	44927918	5.4% (18 d)	5.4% (18 d)
			Aq. photolysis–dark		0.3% (18 d)	0.3% (18 d)
KTU 3072	3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinimine **Formula:** $C_9H_{10}ClN_3S$ **MW:** 227.72 g/mol **SMILES:** ClC1=CC=C(CN2CCSC2=N)C=N1		Anaerobic aquatic	44927935	5.3% (361 d)	5.3% (361 d)

[A] nd means “not detected”. AR means “applied radioactivity”. MW means “molecular weight”. LOQ means “limit of quantitation”. Bolded values are laboratory study values >10%AR.

[*Example*] Table 1.a. Flonicamid and Its Environmental Transformation Products.

Transformation Product Name and Structure	Maximum Percent of Applied Dose (interval)	% of Applied Dose at Final Sampling Interval (Study Duration in Days)	Guideline / MRID	Study Type	Comments
Parent: Flonicamid **CAS. No.:** 158062-67-0 **CAS Name:** N-(Cyanomethyl)-4-(trifluoromethyl)-3-pyridinecarboxamide **IUPAC Name:** N-Cyanomethyl-4-(trifluoromethyl)nicotinamide **Synonyms:** Pyridinecarboxamide, -(cyanomethyl)-4-(trifluoromethyl)-; IKI-220; F-1785 **SMILES:** FC(F)(F)C1=C(C=NC=C1)C(=O)NCC#N 	NA	0 (30 days)	835.4100 / 45854818	aerobic soil metabolism	loamy sand soil, $t_{1/2}$ = 1.2 days (r^2 = 0.90) sandy loam soil, $t_{1/2}$ = 1.2 days (r^2 = 0.91) sand soil, $t_{1/2}$ = 1.9 days (r^2 = 0.99) loamy sand soil, $t_{1/2}$ = 2.4 days (supplementary experiment, 10C)
	NA	18.9% (365 days)	835.4400 / 45854821	anaerobic aquatic metabolism	sandy loam soil, $t_{1/2}$ =166.7 days (r^2 = 0.97; linear) HPLC water, $t_{1/2}$ = 154.6 days (r^2 = 0.95; linear) total system, $t_{1/2}$ = 160.7 days (r^2 = 0.98; linear)
	NA	<LOQ* (375 days; 360 days following the third application)	835.6100 / 45854906 45863811	terrestrial field dissipation	Ephrata, Washington/Quincy loamy fine sand soil $T_{1/2}$ = 3.0 days, DT_{50} = 2.83 days *LOQ = 5.0 µg/Kg
	NA	<LOQ* (282 days; 267 days following the third application)	835.6100 / 45854907 45863811	terrestrial field dissipation	Madera, California/Grangeville fine sandy loam over Traver soils $T_{1/2}$ = 4.0 days, DT_{50} = 2.86 days *LOQ = 5.0 µg/Kg
	NA	<LOQ* (312 days; 297 days following the third application)	835.6100 / 45854908 45863811	terrestrial field dissipation	Northwood, North Dakota/Gardena silt loam soil $T_{1/2}$ = 10.0 days *LOQ = 5.0 µg/Kg
	NA	<LOQ* (285 days; 270 days following the third application)	835.6100 / 45854909 45863811	terrestrial field dissipation	Garner, North Carolina/loamy fine sand $T_{1/2}$ = 10.0 days, DT_{50} = 1.10 days *LOQ = 5.0 µg/Kg
Transformation Product 1: TFNA-OH **CAS No.:** 6-Hydroxy-4-trifluoromethylnicotinic acid	21.3% (3 days), 12.1% (2 days), 17.6% (7 days), 32.7% (7 days)	NA (30 days)	835.4100 / 45854818	aerobic soil metabolism	- loamy sand soil - sandy loam soil - sand soil - loamy sand soil (supplementary experiment, 10C)

Transformation Product Name and Structure	Maximum Percent of Applied Dose (interval)	% of Applied Dose at Final Sampling Interval (Study Duration in Days)	Guideline / MRID	Study Type	Comments
SMILES: OC(=O)C1=C(C=C(O)N=C1)C(F)(F)F 	<5.0 µg/Kg	0 (375 days; 360 days following the third application)	835.6100 / 45854906 45863811	terrestrial field dissipation	Ephrata, Washington/Quincy loamy fine sand soil (detected above the LOQ = 5.0 µg/Kg in one or two assays of replicates).
	5.2% of the total applied in three applications (7 days after 3rd application)	0 (282 days; 267 days after third application)	835.6100 / 45854907 45863811	terrestrial field dissipation	Madera, California/Grangeville fine sandy loam over Traver soils
Transformation Product 2: TFNA **CAS Name:** 4-Trifluoromethylnicotinic acid **SMILES:** OC(=O)C1=C(C=CN=C1)C(F)(F)F 	30.6% (1 day), 19.2% (1 day), 12.2% (3 days), 24.3% (3 days)	NA (30 days)	835.4100 / 45854818	aerobic soil metabolism	- loamy sand soil - sandy loam soil - sand soil - loamy sand soil (supplementary experiment, 10C)
	75.7% (365 days)	75.7% (365 days)	835.4400 / 45854821	anaerobic aquatic metabolism	HPLC water-sandy loam soil (total system)
	7.3% of the total applied in three applications (4 days after 3rd application)	0 (375 days; 360 days after third application)	835.6100 / 45854906 45863811	terrestrial field dissipation	Ephrata, Washington/Quincy loamy fine sand soil
	14.0% of the total applied in three applications (7 days after 3rd application)	0 (282 days; 267 days after third application)	835.6100 / 45854907 45863811	terrestrial field dissipation	Madera, California/Grangeville fine sandy loam over Traver soils

NA = Not analyzed.
ND = Not detected.

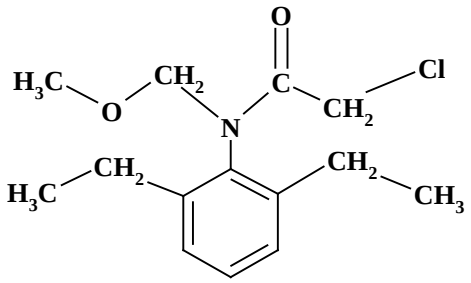
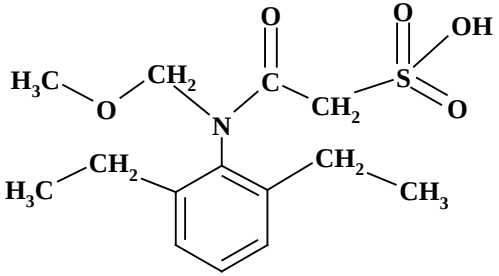
[*Example*] Table 1.b. Summary of Maximum Degradate Amounts in Environmental Fate Studies of [*Chemical Name*].

Degradate [1]	*Max. Degradate % of Applied (Time of Peak)*					*Analyzed Degradates*	
	Hydrolysis	***Aqueous Photolysis***	***Aerobic Soil***	***Anaerobic Aquatic***	***Aerobic Aquatic***	***TFD***	***Ground Water***
[*Degradate 1*]	83% **(30 d)**	40% **(<1, 2 d)**	18-31% **(3-10 d)**	25% **(7 d)**	36-47% **(21-30 d)**		No study
[*Degradate 2*]	10% **(30 d)**	[2]	10-14% **(7-30 d)**	13-17% **(7-21 d)**	06-11% **(30-60 d)**		
[*Degradate 3*]			10-20% **(15-30 d)**	18-22% **(56-180 d)**	16-31% **(100 d)**		
[*Degradate 4*]				~ 1% **(2, 15 d)**			
[*Degradate 5*]		40% **(<1 d)**					
[*Degradate 6*]		19% **(21 d)**					
[*Degradate 7*]		10% **(36 d)**					
[*Degradate 8*]		12% **(36 d)**					
[*Degradate 9*]							

[1] Refer to Example Table 4 for chemical names and structures

[2] Blank cell indicates that degradate was not identified in the corresponding study.

[*Example*] Table 1.c. Chemical Names and Structures of [*Chemical Name*] and Degradation Products Detected in Submitted Environmental Fate Studies.

Name(s)	Structure	Known Chemical and Fate Parameters
[*Chemical Name*] [*Pseudonyms*] [*IUPAC Name*] [*CAS #*] [*SMILES String*]		[brief summary]
[*Degradate 1 Name*] [*Pseudonyms*] [*IUPAC Name*] [*SMILES String*]		None.
[*Degradate 2 Name*] [*Pseudonyms*] [*IUPAC Name*] [*SMILES String*]	[*insert structure*]	None.
[*Degradate 3 Name*] [*Pseudonyms*] [*IUPAC Name*] [*SMILES String*]	[*insert structure*]	None.

Appendix A. Toxicity Comparisons of [*Chemical Name*] and Transformation Products.

The lowest toxicity endpoints for aquatic organisms are listed in **Table A** for the parent compound and any transformation products for which data are available. [*Highlight any compounds of high toxicity class and note any substantial differences of toxicity between the parent compound and the transformation products. Add to Table A toxicity data on transformation products for birds or other taxa not tabulated, if they are available.*]

[*Toxic effects resulting from exposure to chemicals with a similar mode of action are usually a function of the number of molecules and thus it is appropriate to compare toxicity on the basis of molar mass, especially when molecular weight differs substantially (*e.g.*, several fold) between the two compounds (Rand, 2003). Expressing the endpoints on a parent equivalents basis is essentially equivalent to the expression of the endpoint on a molar basis, it is simply normalized to the parent compound's molecular weight rather than to moles.*]

Table A. Toxicity Comparison of Parent Compound and Transformation Products.[A]

Test Material	MW (g/mol)	Test Species	Endpoint	Toxicity Value in mg/L (95% Confidence Interval)	Degradate Toxicity Expressed in Parent Compound Equivalents in mg/L (95% Confidence Interval) [B]
Freshwater Fish					
[*Parent compound*]	359.42	Rainbow trout (*O. mykiss*)	96-hr LC_{50}	0.39 (0.22-0.55)	0.39 (0.22-0.55)
[*Product 1*]	180.08	Rainbow trout (*O. mykiss*)		>99	>198
[*Product 2*]	194.11	Bluegill sunfish (*L. macrochirus*)		>97	>179
[*Product 3*]	193.13	Rainbow trout (*O. mykiss*)		>100	>187
[*Product 4*]	375.42	Rainbow trout (*O. mykiss*)		>9.3	>8.9
[*Product 5*]	391.41	Rainbow trout (*O. mykiss*)		4.8 (4.2-5.5)	4.6 (4.0-5.2)
Freshwater Invertebrates					
[*Parent compound*]	359.42	*D. magna*	48-hr EC_{50}	2.5 (2.3-2.7)	2.5 (2.3-2.7)
[*Product 1*]	180.08	*D. magna*		>99	>198
[*Product 2*]	194.11	*D. magna*		>92	>170
[*Product 3*]	193.13	*D. magna*		>101	>187
[*Product 4*]	375.42	*D. magna*		>8.7	**>8.3**
[*Product 5*]	391.41	*D. magna*		>4.5	**>4.1**
Aquatic Plants					
[*Parent compound*]	359.42	Green alga (*P. subcapitata*)	96-hr EC_{50}	1.6 (1.3-1.9)	1.6 (1.3-1.9)
[*Product 1*]	180.08	Green alga (*P. subcapitata*)		>86	>171
[*Product 2*]	194.11	Green alga (*P. subcapitata*)		83 (75-91)	154 (139-169)
[*Product 3*]	193.13	Green alga (*P. subcapitata*)		>100	>187
[*Product 4*]	375.42	Green alga (*P. subcapitata*)		>8.4	**>8.1**
[*Product 5*]	391.41	Green alga (*P. subcapitata*)		1.8 (1.6-2.0)	**1.7 (1.4-1.9)**

[A] **Bold** values indicate degradate toxicity that is potentially equivalent to the parent compound (*i.e.*, the toxicity of the parent compound and the degradate are within an order of magnitude or the confidence intervals overlap or both). **Bold red** values indicate degradate toxicity that is potentially substantially greater than that of the parent compound.

[B] Degradate toxicity in parent compound equivalents (mg/L) = (MW parent/MW degradate) x (toxicity endpoint of degradate (mg/L)).

[*If ECOSAR is used to estimate degradate toxicity, then Table B and the paragraph below may be added to the memorandum. Include a brief introduction to Table B, including how the toxicity values were calculated. Some example text is provided below.*]

ECOSAR (v1.0) was used to estimate the toxicity of the transformation products listed in **Table B** because study data were not available with which to evaluate their toxicity. ECOSAR predicts toxicity using a regression of the log K_{OW} and measured toxicity endpoints for a particular species and chemical class. ECOSAR is only used to prioritize the need for additional data on transformation products. Data on the [*XXX*] and [*XXX*] chemical classes were used to estimate toxicity endpoints (see the description of data in the Help section of ECOSAR). Very limited data sets were available to develop the regressions for the compounds and there is large uncertainty in the estimated values. However, this is one of the best methods available to estimate ecological toxicity.

Table B. ECOSAR Estimates of Transformation Product Toxicity. [A]

Compound (Chemical Class) [C]	Estimated Toxicity Value (mg/L)				
	96-hr FW fish EC_{50}	**48-hr FW Daphnid LC_{50}**	**Fish NOAEC**	**Daphnid NOAEC**	**96-hr EC_{50} Green Algae**
[*Parent compound*] [B] (Chemical class)	(>122, >142)	(>97.3, >129)	(6.5)	(6.1)	(6.2)
[*Product 1*] (Chemical class)	(100) 5.32×10^5	47315	624	(0.1) 3148	16.6
[*Product 2*] (Chemical class)	3754	853	11.3	22.2	2.9
[*Product 3*] (Chemical class)	156	3.2	0.08	0.9	1.0
[*Product 4*] (Chemical class)	78.9	2.4	0.05	0.4	9.2
[*Product 5*] (Chemical class)	124	6.5	0.11	1.5	8.9

[A] Toxicity values in parentheses were measured. All other toxicity values were estimated with ECOSAR (v1.0).

[B] Toxicity values for the parent compound were not estimated because the transformation products are in a different chemical class and are assumed to have a different mode of action.

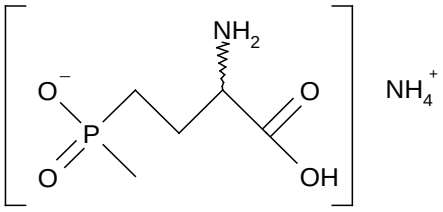
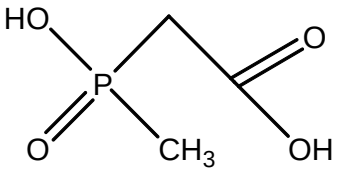
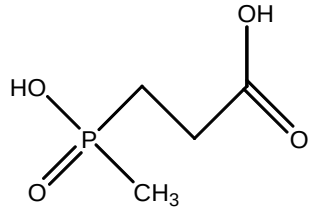
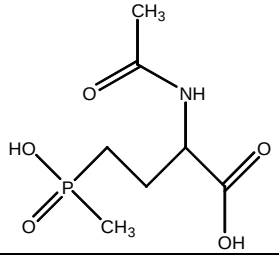
[C] Chemical class used by ECOSAR to predict toxicity.

Rand, G. M. 2003. *Aquatic Toxicology* (Second ed.). London: Taylor & Francis.

[*Example*] Appendix B. One-Sheet Summary of the Chemical Properties and Environmental Fate Parameters of Glufosinate ammonium

Molecular weight: 198.2 g/mol
Solubility (water, 20°C): 1.37×10^{6} mg/L
Vapor pressure (25°C): $<7.5 \times 10^{-9}$ torr
K_{OW}: <0.1
K_{OC}: mobile to moderately mobile (17-605 mL/g_{oc})
Hydrolysis: stable
Aqueous photolysis: stable
Soil photolysis: 17 days
Aerobic soil: 9-23 days
Anaerobic soil: 37 days
Aerobic aquatic: 1-87 days
TFD: 8-23 days
AFD: <7 days (1st app to soil, LA), 154 days (2nd app to soil, LA), 3 days (2 apps to flooded soil, CA)
USGS NAWQA: SW - detected 6/1150 times, max. 3.23 µg/L
GW – detected 6/827 times, max. 4.49 µg/L

Structure of glufosinate ammonium and major degradates

Glufosinate ammonium (parent) **Name:** Ammonium-(2RS)-2-amino-4-(methylphosphinato)butyric acid 	**MPA (HOE 064619)** **Name:** 2-methylphosphinico-acetic acid 
MPP (HOE 061517) **Name:** 3-methylphosphinico-propionic acid 	**NAG (HOE 085355/HOE 099730)** **Name:** 2-acetamido-4-methylphosphinico-butanoic acid 

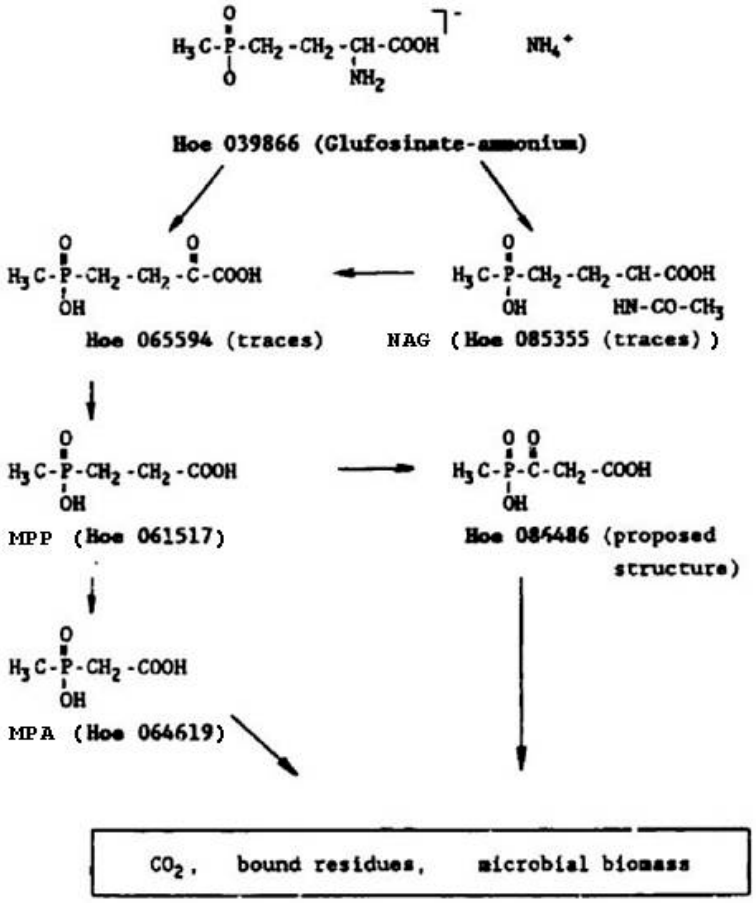
Summary of maximum major degradate amounts in environmental fate studies

Study Type	MRID	Maximum percentage (day)		
		MPP HOE 061517	**MPA HOE 064619**	**NAG HOE 085355/ HOE 099730**
Hydrolysis (%)	40345656	NA	NA	NA
Aqueous Photolysis (%)	41323115	NA	NA	NA
Soil Photolysis (%)	41920102	**60.4** (Day 30*)	8.5 (Day 16)	**17.7** (Day 4)
Aerobic Soil (%)	41323119			
	Sandy loam	**47.7** (Day 7)	**28.2** (Day 14)	ND
	Silt loam	**25.8** (Day 14)	3.1 (Day 20)	ND
	Loamy sand	**36.5** (Day 7)	**10.7** (Day 20)	ND
	40345659A			
	Sandy loam	**42.5** (Day 64)	6.6 (Day 98)	ND
	Sandy loam	**55.4** (Day 64)	**10.3** (Day 95*)	ND
	Silt loam	**41.7** (Day 64)	**18.5** (Day 95*)	ND

Study Type	MRID	Maximum percentage (day)		
		MPP HOE 061517	**MPA HOE 064619**	**NAG HOE 085355/ HOE 099730**
Anaerobic Soil (%)	40501014	**42.2** (Day 60*)	5.8 (Day 60*)	ND
Aerobic Aquatic (%)	40345660			
	Silt loam	**16.5** (Day 64)	**18.4** (Day 94*)	ND
	Sand	**56.5** (Day 64)	**19.1** (Day 94*)	ND
	45204402/01			
	Loam	**48.4** (Day 91)	**19.9** (Day 50)	8.2 (Day 7)
	Sand (1ppm)	**30.5** (Day 50)	**15.5** (Day 130*)	4.3 (Day 50)
	Sand (0.1 ppm)	**79.8** (Day 14)	6.8 (Day 130*)	9.9 (Day 1)
Anaerobic Aquatic (%)	46258601	ND	ND	ND
Terrestrial Field Dissipation (ppm)	43110402	0.172 (Day 192)	0.055 (Day 184)	NA
	43766915	0.21 (Day 42)	0.11 (Day 296)	NA
	43766916	0.15 (Day 14)	0.10 (Day 45)	NA
	47542601	0.10 (Day 28)	0.05 (Day 65)	NA
Aquatic Field Dissipation (ppm)	45204403			
	CA	0.014 (Day 18)	0.002 (Day 18)	NA
	LA	0.188 (Day 18)	0.032 (Day 18)	NA

ND – not detected. NA - Not analyzed.
* Day reflects end of study period.

Proposed degradation pathway



EFED/HED Collaboration on Drinking Water Degradates of Concern
Preparation of Preliminary Work Plan for Registration Review
January 2013

There have been delays during the preparation of problem formulation/scoping documents when new degradates have been identified during problem formulation that have the potential for human exposure in drinking water. OPP may identify potential data gaps for these degradates; ideally OPP should further explore whether these degradates are really of concern for human or environmental exposure prior to levying these requirements. A workgroup consisting of members from the Residues of Concern Knowledge-based Subcommittee (ROCKS) has developed a suggested process for addressing these concerns.

Suggested Process:

1) At the initial team meeting HED should provide EFED with a listing of all degradates that have been included in the most recent drinking water dietary exposure assessment. In addition, HED should provide EFED with a reference to the memorandum that provides the rationale for inclusion of these degradates in the drinking water assessment (DWA). This reference could be a committee recommendation memorandum (ROCKS, MARC[1]) or a human health risk assessment with a detailed rationale for inclusion/exclusion of degradates. If there is NOT a good reference on the drinking water residues of concern (DWROC) or if HED has concerns about the previous decision HED will alert EFED. The HED and EFED representatives may want to set up a separate meeting soon thereafter to discuss the DWROC if there are significant concerns about the previous decision (or lack thereof).

2) Within four weeks of the due date EFED will review their database and determine if additional fate or other information has been received since the last risk assessment. EFED will send an email to HED with a discussion on whether the DWROC may need updating. Potential conclusions include (but are not limited to) the following:

- No additional fate data have been received and there is no indication that the previous determination of degradates that are included/excluded in the DWA should be modified due to changes in use patterns;
- Additional fate or other data have been received and there are additional major degradates have been identified.

3) If there are indications that the residues of concern decision needs to be revisited, EFED should send HED a list of the major environmental degradates that could reach drinking water along with the chemical structures and relative amounts.

4) The HED/EFED Registration Review team will review listing and attempt to determine those degradates that should be included in the DWA. The team will consider similarity in chemical structures to other degradates, if the new degradates may already be included in the food dietary risk assessment, and available toxicity data on degradates. Structure-activity tools and databases such as DEREK NEXUS and METAPATH may be used.

[1] MARC = Metabolism Assessment Review Committee

5) If the team cannot come to a conclusion, they will consult with the ROCKS co-chairs to determine the need for an electronic review or ad hoc meeting. The ROCKS co-chairs will send an email with their recommendation.

6) HED will send an email with the revised recommendation on residues of concern with a rationale. EFED will use that rationale as the basis for any additional degradate data requirements. HED will document the revised recommendation in the Scoping Document.

7) If there doesn't appear to be a need to re-evaluate residues of concern EFED will send HED an email with a discussion on whether the most recent DWA will need modification at the time of registration review due to changes in models or use patterns. HED will make a note of the need for a revised DWA in the scoping document. HED usually includes a qualifier on the potential for updating the dietary risk assessment with revised drinking water values.

Note: The HED/EFED team for developing the documents for the preliminary work plan should ensure that the DWROC considerations are documented for the reg review risk assessment team. In some cases the team DWROC decision will need to be deferred until additional fate data are submitted. Further guidance on incorporation of drinking water considerations in the preliminary reg review risk assessment will be forthcoming.

EFED/HED Registration Review Flow Chart – Drinking Water Degradates of Concern (DWROC) for Preliminary Work Plan – January 2013